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Effectiveness of Radiation Therapy Alone for Elderly Patients with Unresected Stage III Non-Small Cell Lung Cancer

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Abstract

Purpose—Chemoradiotherapy is the standard of care for unresectable stage III non-small cell lung cancer (NSCLC). Elderly patients, who are often considered unfit for combined chemoradiotherapy, frequently receive radiation therapy (RT) alone. Using population-based data, we evaluated the effectiveness and tolerability of lone RT in unresected elderly stage III NSCLC patients.

Methods and Materials—Using the Surveillance, Epidemiology and End Results (SEER) registry linked to Medicare records we identified 10,376 cases of unresected stage III NSCLC that were not treated with chemotherapy, diagnosed between 1992 and 2007. We used logistic regression to determine propensity scores for RT treatment using patients' pre-treatment characteristics. We then compared survival of patients who underwent lone RT vs. no treatment using a Cox regression model adjusting for propensity scores. The adjusted odds for toxicity among patients treated with and without RT were also estimated.

Results—Overall, 6,468 (62%) patients received lone RT. Adjusted analyses showed that RT was associated with improved overall survival in unresected stage III NCSLC (hazard ratio [HR]: 0.76; 95% confidence interval [CI]: 0.74–0.79) after controlling for propensity scores. RT treated patients had an increased adjusted risk of hospitalization for pneumonitis (odds ratio [OR]: 89, 95% CI: 12–636), and esophagitis (OR: 8, 95% CI: 3–21).

Conclusions—These data suggest that use of RT alone may improve the outcomes of elderly patients with unresected stage III NSCLC. Severe toxicity, however, was considerably higher in the RT treated group. The potential risks and benefits of RT should be carefully discussed with eligible elderly NSCLC patients.

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Conflicts of Interest
None declared.

Keywords

Non-small cell lung cancer; Radiotherapy; Lone Radiotherapy; Elderly; Outcomes; Toxicity; Unresectable lung cancer

Background

In the United States, approximately 40% of new non-small cell lung cancer (NSCLC) cases present with locally advanced, stage III disease.[1] Many of these cases, including those staged IIIA with mediastinal (N2) lymph node involvement or with stage IIIB disease, are considered inoperable. Concurrent platinum-based chemotherapy and radiotherapy (RT) has been associated with the greatest survival benefits in these patients.[2, 3] However, RT is still frequently administered alone, without chemotherapy, to elderly patients who are not candidates for dual modality therapy. Although increasing evidence suggests that elderly NSCLC patients tolerate chemotherapy well, guidelines suggest considering lone radiotherapy in patients with unresected stage III disease and performance status >2. [4, 5]

Long-term survival associated with RT monotherapy in inoperable stage III NSCLC is poor, estimated at around 5%.[2] Goals of RT in this setting are to improve symptoms associated with advanced lung cancer as well as potentially extend patient survival. Data exist demonstrating improvement in symptoms with RT alone[6, 7], however, mortality benefits are less clear. No randomized control trials (RCTs) comparing modern RT to placebo in locally advanced NSCLC have been performed. Several RCTs have evaluated survival in RT administered without chemotherapy by comparing different radiation schedules and dosing intensities. A systematic review published in 2008 reported mixed results, with some trials demonstrating survival benefits associated with intensive RT dosing and others finding no mortality benefits.[7]

RT can be associated with severe toxicities including pneumonitis and esophagitis, and also rarely cardiac and spinal cord toxicity.[8, 9] Elderly patients may be at higher risk of RT-mediated toxicity because of a greater burden of comorbid illnesses and reduced functional organ reserve.[10, 11] There is limited data from clinical trials regarding RT related toxicity in the elderly and therefore few conclusions can be made regarding tolerability.

In this study, we used nationally representative data to evaluate the potential survival benefits and adverse events associated with lone RT in inoperable, elderly stage III NSCLC patients.

Methods

Our study used data from the Surveillance, Epidemiology, and End Results (SEER) registry linked to Medicare claims. From this database we identified all cases of primary stage III NSCLC diagnosed prior to autopsy in patients age >65 years between 1992 and 2007. We defined patients as “elderly” if they were older than age 65, as this age criteria has been used in many previous cancer studies, and also as this specific age group (age >65 years) has been underrepresented in oncology clinical trials.[12] We limited our study cohort to patients who were not considered candidates for resection including stage IIIA cases with N2 lymph node disease or stage IIIB according to the Tumor, Node, Metastases, 7th edition classification. [13] We then excluded cases treated with surgical resection or that received any form of chemotherapy. We also excluded patients who died within 4 weeks of their cancer diagnosis and those who were residing in nursing homes or enrolled in hospice care as they would have been unlikely to receive RT. Our final analytic sample included 10,376 patients.

Sociodemographic variables (age, sex, race/ethnicity, and marital status) and tumor characteristics (location, size, stage, and histology) were obtained from SEER. Income was estimated based on patients' census data or zip code provided in Medicare. Using Medicare data, we calculated modified Charlson scores to quantify patients' burden of comorbid illnesses. Data on patients' diagnostic evaluation including use of mediastinoscopy and positron emission tomography scanning were collected from Medicare claims files. We identified Medicare claims for home health care, which we used as a marker for poor functional status, as only homebound patients are eligible for these services.

We ascertained treatment with RT using SEER data and Medicare claims. A patient was coded as having received RT if SEER data indicated use of external beam radiation or if Medicare inpatient, outpatient or physician claims were consistent with RT administration.[14] Complexity of radiation was ascertained from Medicare claims. RT complexity refers to the number of portals and volumes of interest used in setting a radiation field as well as the complexity of the planning scheme (i.e. simple two-dimensional techniques for "simple" and "intermediate" complexity, versus three-dimensional (3D) reconstructions for "complex" planning schemes.) We used the following categorizations: "simple" (simulation and planning of a single treatment area with either a single portal or parallel opposed portals; Current Procedural Terminology-4 [CPT] codes 77261 and 77280), "intermediate" (simulation and planning involving three or more portals or two separate treatment areas with multiple blocks; CPT-4 codes 77262 and 77285) and "complex" (simulation and planning involving tangential portals, three or more treatment areas, rotation or arc therapy, complex or custom blocks and/or 3D reconstructed imaging using CT or MRI data or intensity-modulated RT; CPT-4 codes 77263, 77290, 77295 or 77301).[15, 16]

We used a published algorithm to find episodes of serious esophagitis and pneumonitis requiring hospitalization related to RT administration.[17] Survival time was calculated using the date of cancer diagnosis until the date of death or loss to follow-up. Overall survival analyses used Medicare death data and were censored on December 31, 2009. Lung cancer-specific survival analyses were censored on December 31, 2007. Data on cause of death was collected from SEER based on International Classification of Disease 9th Edition diagnostic codes.

Statistical Analysis

We compared baseline characteristics of patients treated with lone RT to untreated individuals using the chi-squared test. Overall survival (OS) and lung cancer-specific survival were compared in those who received RT to those who did not using Kaplan-Meier methods.

Propensity scores for treatment with RT alone were generated using a logistic regression that included sociodemographic characteristics, comorbidity score, use of home health services, diagnostic tests, and tumor characteristics as covariates.

To assess the adjusted association of RT administration and prognosis, we used Cox regression with OS or lung cancer specific-survival as outcomes, adjusting for propensity scores. To confirm our findings, we used Cox models stratified by propensity score quintiles and marginal Cox models for correlated data, matching patients treated with and without RT by their propensity score.[18] We performed secondary analyses stratifying the sample by stage (IIIA vs. IIIB) and RT complexity (intermediate vs. high complexity). Additionally we conducted analyses adjusting for year of diagnosis to control for potential temporal changes in the outcomes of patients with lung cancer.

We used logistic regression to calculate unadjusted odds of severe adverse events in patients treated with RT, and then adjusted these analyses for propensity scores. We also compared rates of severe adverse events by level of RT planning complexity using logistic regression.

Based on the number of deaths observed among patients in the cohort, we estimated that the study had an 80% power to detect a hazard of death associated with RT of approximately 0.94 at a 0.05 significance level. All analyses were performed in SAS version 9.2 (SAS, Cary, NC). This study was approved by the Mount Sinai Institutional Review Board (Approval 07–0091).

Results

Overall, 62% (n=6,468; 95% confidence interval [CI]: 61–63) of elderly patients in our sample were treated with lone RT. Patients treated with RT were more likely to be male (p=0.003), married (p=0.0003), white (p=0.03) and living in higher income areas (p=0.04; Table 1). Tumors treated with RT tended to be larger in size (p<0.0001), located in the upper lung lobes (p<0.0001), and of squamous cell histology (p<0.0001). Patients receiving RT also had lower co-morbidity scores (p=0.0001). The distribution of covariates was well balanced after adjustment for propensity scores (Table 1). Median follow-up was 9 months (Interquartile range [IQR]: 4 – 17 months) for patients treated with lone RT and 8 months (IQR: 3–18 months) for patients who received no treatment.

The median OS for patients receiving RT was 9.0 (95% CI: 8.7–9.3) months compared to 7.0 (95% CI: 6.6–7.4) months for untreated patients. Kaplan-Meier analyses showed improved overall (p<0.001) and lung-cancer specific survival (p=0.005) in the entire cohort as well as with both stage IIIA and stage IIIB NSCLC cases.

In analyses including all stage III patients, RT was associated with an improvement in overall (hazard ratio [HR]: 0.87; 95% CI: 0.83–0.91) and lung cancer-specific (HR 0.90; 95% CI: 0.85–0.93) survival in propensity score adjusted models (Table 2). A similar benefit was noted in models stratified by propensity score quintiles as well as a propensity score-matched analysis, and in analyses adjusted by year of cancer diagnosis. Results of confirmatory analyses and analyses stratified by RT planning complexity were similar. Analyses comparing patients receiving intermediate complexity planning to those not receiving RT showed no overall (HR 1.05; 95% CI: 0.99–1.11) or lung cancer-specific (HR 1.02; 95% CI: 0.97–1.09) survival benefit associated with RT. Conversely, high complexity RT planning was associated with a significant improvement in both overall (HR: 0.83; 95% CI: 0.76–0.90) and lung cancer-specific (HR 0.87; 95% CI: 0.79–0.95) survival. Analyses stratified by tumor stage revealed an OS benefit associated with RT in stage IIIA (adjusted HR 0.83; 95% CI: 0.78–0.88) and stage IIIB (HR 0.90; 95% CI: 0.85–0.96) disease.

RT was associated with severe adverse events leading to inpatient hospitalization (Table 3). Patients treated with RT were significantly more likely to experience pneumonitis (2.2% vs. <1%; adjusted odds ratio [OR]: 88, 95% CI: 12–636) and esophagitis (1.1% vs. <1%; adjusted OR: 8, 95% CI: 3–21). When comparing intermediate versus high complexity regimens, no significant difference was noted in rates of pneumonitis (3.3% vs. 3.5%; p>0.05) or esophagitis (1.5% vs. 1.9%; p>0.05).

Discussion

In patients with stage III NSCLC, RT is often administered alone to elderly individuals who are not considered candidates for combined chemoradiation. There is limited evidence demonstrating a direct survival benefit associated with RT alone in these patients, particularly using newer modalities. In this population-based study, we found that RT use

was associated with a modest survival benefit, and that this benefit was limited to patients treated with high complexity regimens. RT treatment was also associated with an increased risk of serious adverse events. While these findings should be interpreted with caution given the possibility of selection bias, they suggest that increased use of RT alone may improve survival of elderly patients with stage III disease who are not candidates for combined chemoradiation.

A single RCT from the 1960s has been conducted comparing RT to no treatment in inoperable NSCLC, finding no significant survival benefit associated with RT.[19] Since then, RT techniques have evolved from simple, one-dimensional planning to two-, and three-dimensional techniques and more recently, intensity modulated RT. However, no RCTs exist evaluating the potential effectiveness and tolerability of newer RT techniques compared with no treatment. A number of clinical trials of lone RT therapy have randomized patients to different dosing schedules and intensity; a survival benefit has been observed in some of these trials associated with higher RT doses or more frequent administrations, but improvements in mortality have not been consistent between trials.[20–22] Moreover, clinical trials evaluating the effectiveness of different RT regimens have included younger NSCLC patients, limiting generalizability of these data to the elderly. One retrospective single-center study has reported their experience with elderly patients with unresectable stage III NSCLC and found a significantly increased survival with higher doses of RT.[23]

Combined chemotherapy and RT is the preferred treatment in unresectable NSCLC. The European Organization for the Research and Treatment of Cancer conducted the largest trial comparing chemoradiotherapy to lone RT in inoperable NSCLC and found a significant survival benefit associated with the use of concomitant platinum chemotherapy with RT.[24] A Cochrane meta-analysis pooling data from nine trials has confirmed these results.[25] These trials support the use of dual modality therapy in appropriate candidates, but provide limited information to guide use of combined chemoradiation in older patients. However, a recent RCT of chemoradiation vs. RT in elderly patients demonstrated that dual modality therapy was relatively well tolerated and associated with a survival benefit.[3] Elderly patients considered to be ineligible for chemotherapy are likely to be frail or to have a limited performance status, thus it is unlikely that future randomized trials of RT monotherapy will be performed in this patient group. Lung cancer is a disease of the elderly; the mean age at NSCLC diagnosis is 70, and the majority of cases are inoperable on discovery. Thus, our study helps inform clinical decision making for a large number of elderly patients whose clinical characteristics have been underrepresented in clinical trials.

In analyses where we evaluated the effects of RT stratified by level of planning complexity, we found a significant survival benefit with high complexity regimens but no clear improvement in survival in patients who underwent intermediate complexity planning. These findings are consistent with a previous study of SEER-Medicare data that found improved survival with increasing levels of RT complexity in stage IIIB NSCLC patients treated with chemoradiotherapy.[15] Similarly, higher complexity RT regimens have been shown to lead to markedly improved outcomes in inoperable early stage NSCLC.[26] However, no RCT data exists comparing the impact of RT complexity on clinical outcomes of patients with lung cancer. Our study provides additional evidence that newer, more complex planning and simulation RT techniques lead to better lung cancer outcomes.

We found that patients who received RT were more likely to experience severe adverse events requiring hospitalization, including esophagitis and pneumonitis. Despite the markedly enhanced risk for these complications in RT treated patients, the overall rates of esophagitis and pneumonitis leading to hospitalization were low. This finding is consistent

with a case series of 48 inoperable elderly NSCLC patients, which reported no episodes of significant pneumonitis or esophagitis.[23] Thus, the benefits of RT appear to outweigh the potential negative impact of treatment on the quality of life of elderly stage III NSCLC patients. However, additional data is needed to fully assess the extent of the effect of RT on the quality of life of these patients, including the need for multiple treatment visits and the impact of less severe toxicity causing pain and discomfort but not requiring hospitalization.

A strength of this study is the use of a large, nationally representative sample with long-term follow-up. The patients included in the cohort represent a diverse group of elderly NSCLC patients, as opposed to many smaller case series from single institutions. These data reflect treatment outcomes in “real world” patients, providing a different perspective from clinical trials.

A limitation of our work was the use of observational data to assess the potential benefit of RT alone in the elderly. Patients in our cohort were assigned to RT or no treatment based on patient characteristics, physician recommendation, and patients preferences, creating unbalanced comparison arms. The impact of these factors on prognosis potentially confounds the observed effects of RT on survival. To minimize bias, we used propensity scores, generated by measured baseline patient and tumor characteristics. Although this methodology can help to account for some factors that may have affected the decision to administer RT, it cannot adjust for unmeasured confounders. However, our analyses showed that the beneficial effect of RT was limited to patients treated with high complexity planning suggesting that our results are not due to selective use of RT among patients with favorable prognostic factors. We also could not adjust for RT dose, as this data is not available in SEER-Medicare. Thus, our analytic plan mimics an intent-to-treat analysis, by comparing patients treated with and without RT, regardless of the total dose received. A further limitation of our study is that we had no formal classification of radiotherapy associated toxicities, although we used a previously published method for identifying toxicities serious enough to require hospitalization. This method has been suggested as a standardized way of evaluating cancer treatment toxicities, as hospitalization is likely to represent pneumonitis and esophagitis grade three or worse. Furthermore, treatment toxicities are under-reported outside of rigorous clinical trials, necessitating alternative methods for ascertaining these important outcomes.[17]

In summary, RT mono-therapy is frequently used to treat inoperable elderly stage III NSCLC patients who are not candidates for aggressive chemoradiotherapy. These data suggest that RT is associated with improved survival in this population despite increased risks of toxicity. Although results from RCTs are needed to confirm these results, physicians should discuss the potential risks and benefits of this therapy with their elderly stage III lung cancer patients.

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Abbreviations and Acronyms

NSCLC	non-small cell lung cancer
SEER	Surveillance, Epidemiology and End Results
RT	radiotherapy
RCT	randomized controlled trial
PET	positron emission tomography
CPT	Current Procedural Terminology
OS	overall survival
CI	confidence interval
OR	odds ratio
HR	hazard ratio

References

1. Mountain CF. Revisions in the International System for Staging Lung Cancer. Chest. 1997; 111:1710–1717. [PubMed: 9187198]
2. Sause W, Kolesar P, Taylor SI, Johnson D, Livingston R, Komaki R, Emami B, Curran W Jr, Byhardt R, Dar AR, Turrisi A 3rd. Final results of phase III trial in regionally advanced unresectable non-small cell lung cancer: Radiation Therapy Oncology Group, Eastern Cooperative Oncology Group, and Southwest Oncology Group. Chest. 2000; 117:358–364. [PubMed: 10669675]
3. Atagi S, Kawahara M, Yokoyama A, Okamoto H, Yamamoto N, Ohe Y, Sawa T, Ishikura S, Shibata T, Fukuda H, Saijo N, Tamura T. Thoracic radiotherapy with or without daily low-dose carboplatin in elderly patients with non-small-cell lung cancer: a randomised, controlled, phase 3 trial by the Japan Clinical Oncology Group (JCOG0301). Lancet Oncol. 2012:671–678. [PubMed: 22622008]
4. Booton R, Jones M, Thatcher N. Lung cancer 7: management of lung cancer in elderly patients. Thorax. 2003; 58:711–720. [PubMed: 12885992]
5. Ramnath N, Dilling TJ, Harris LJ, Kim AW, Michaud GC, Balekian AA, Diekemper R, Detterbeck FC, Arenberg DA. Treatment of Stage III Non-small Cell Lung Cancer: Diagnosis and Management of Lung Cancer, 3rd ed: American College of Chest Physicians Evidence-Based Clinical Practice Guidelines. Chest. 2013; 143:e314S–340S. [PubMed: 23649445]
6. Brundage MD, Bezjak A, Dixon P, Grimard L, Larochelle M, Warde P, Warr D. The role of palliative thoracic radiotherapy in non-small cell lung cancer. Can J Oncol. 1996; 6 (Suppl 1):25–32. [PubMed: 8853535]
7. Fairchild A, Harris K, Barnes E, Wong R, Lutz S, Bezjak A, Cheung P, Chow E. Palliative thoracic radiotherapy for lung cancer: a systematic review. J Clin Oncol. 2008; 26:4001–4011. [PubMed: 18711191]
8. Wisnivesky JP, Bonomi M, Lurslurchachai L, Mhango G, Halm EA. Radiotherapy and Chemotherapy for Elderly Patients with Stage I-II Unresected Lung Cancer. Eur Respir J. 2012
9. Perry, M.; Yarbro, J. Toxicity of Chemotherapy. Orlando, FL: Grune and Straton; 1984.
10. Repetto L, Balducci L. A case for geriatric oncology. Lancet Oncol. 2002; 3:289–297. [PubMed: 12067806]
11. Havlik RJ, Yancik R, Long S, Ries L, Edwards B. The National Institute on Aging and the National Cancer Institute SEER collaborative study on comorbidity and early diagnosis of cancer in the elderly. Cancer. 1994; 74:2101–2106. [PubMed: 8087777]
12. Hutchins LF, Unger JM, Crowley JJ, Coltman CA Jr, Albain KS. Underrepresentation of patients 65 years of age or older in cancer-treatment trials. N Engl J Med. 1999; 341:2061–2067. [PubMed: 10615079]

13. Detterbeck FC, Boffa DJ, Tanoue LT. The new lung cancer staging system. Chest. 2009; 136:260–271. [PubMed: 19584208]

14. Virnig BA, Warren JL, Cooper GS, Klabunde CN, Schussler N, Freeman J. Studying radiation therapy using SEER-Medicare-linked data. Med Care. 2002; 40:IV-49–54.

15. Goldsmith B, Cesaretti J, Wisnivesky JP. Radiotherapy Planning Complexity and Survival after Treatment of Advanced Stage Lung Cancer in the Elderly. Cancer. 2009; 115:4865–4873. [PubMed: 21423827]

16. Park CH, Bonomi M, Cesaretti J, Neugut AI, Wisnivesky JP. Effect of radiotherapy planning complexity on survival of elderly patients with unresected localized lung cancer. Int J Radiat Oncol Biol Phys. 2011; 81:706–711. [PubMed: 20932683]

17. Du XL, Osborne C, Goodwin JS. Population-based assessment of hospitalizations for toxicity from chemotherapy in older women with breast cancer. J Clin Oncol. 2002; 20:4636–4642. [PubMed: 12488407]

18. Wei L, Lin D, Weissfeld L. Regression analysis of multivariate incomplete failure time data by modeling marginal distributions. J Am Stat Assoc. 1989; 84:1065–1063.

19. Roswit B, Patno M, Rapp R, Veinbergs A, Feder B, Stuhlbarg J, Reid C. The survival of patients with inoperable lung cancer: a large-scale randomized study of radiation therapy versus placebo. Radiology. 1968; 90:688–697. [PubMed: 4170866]

20. Kepka L, Olszyna-Serementa M. Palliative thoracic radiotherapy for lung cancer. Expert Rev Anticancer Ther. 2010; 10:559–569. [PubMed: 20397921]

21. Sause WT, Scott C, Taylor S, Johnson D, Livingston R, Komaki R, Emami B, Curran WJ, Byhardt RW, Turrisi AT, et al. Radiation Therapy Oncology Group (RTOG) 88-08 and Eastern Cooperative Oncology Group (ECOG) 4588: preliminary results of a phase III trial in regionally advanced, unresectable non-small-cell lung cancer. J Natl Cancer Inst. 1995; 87:198–205. [PubMed: 7707407]

22. Perez CA, Stanley K, Rubin P, Kramer S, Brady L, Perez-Tamayo R, Brown GS, Concannon J, Rotman M, Seydel HG. A prospective randomized study of various irradiation doses and fractionation schedules in the treatment of inoperable non-oat-cell carcinoma of the lung. Preliminary report by the Radiation Therapy Oncology Group. Cancer. 1980; 45:2744–2753. [PubMed: 6991092]

23. Lonardi F, Coeli M, Pavanato G, Adami F, Gioga G, Campostrini F. Radiotherapy for non-small cell lung cancer in patients aged 75 and over: safety, effectiveness and possible impact on survival. Lung Cancer. 2000; 28:43–50. [PubMed: 10704708]

24. Schaake-Koning C, van den Bogaert W, Dalesio O, Festen J, Hoogenhout J, van Houtte P, Kirkpatrick A, Koolen M, Maat B, Nijs A, et al. Effects of concomitant cisplatin and radiotherapy on inoperable non-small-cell lung cancer. N Engl J Med. 1992; 326:524–530. [PubMed: 1310160]

25. O'Rourke N, Roque IFM, Farre Bernado N, Macbeth F. Concurrent chemoradiotherapy in non-small cell lung cancer. Cochrane Database Syst Rev. 2010; 1:1–47.

26. Timmerman R, Paulus R, Galvin J, Michalski J, Straube W, Bradley J, Fakiris A, Bezjak A, Videtic G, Johnstone D, Fowler J, Gore E, Choy H. Stereotactic body radiation therapy for inoperable early stage lung cancer. JAMA. 2010; 303:1070–1076. [PubMed: 20233825]

Table 1

Baseline Characteristics of Unresected Stage III Elderly NSCLC Cohort Treated with and Without Radiotherapy.

Characteristic	Radiation Therapy (N=6,468)	No Treatment (N=3,908)	*P*-value	
			Unadjusted	Adjusted*
Age, years, n (%)			0.07	0.7
≤69	1,619 (25)	908 (23)		
70–75	2,167 (34)	1,306 (33)		
>75	2,682 (41)	1,694 (44)		
Female, n (%)	2,534 (39)	1,645 (42)	0.003	0.9
Race, n (%)				
White	5,085 (78)	2,983 (76)	0.03	0.9
African American	650 (10)	434 (11)		
Hispanic	291 (5)	214 (6)		
Other	442 (7)	277 (7)		
Marital Status				
Married	3,521 (54)	1,985 (51)	0.0003	0.9
Estimated Median Income, n (%)				
Highest three quartiles	4,786 (74)	2,807 (72)	0.04	0.9
Lowest quartile	1,682 (26)	1,101 (28)		
Tumor Location, n (%)				
Upper lobe	3,823 (59)	2,109 (54)	<0.0001	0.9
Middle lobe	222 (3)	150 (4)		
Lower lobe	1,328 (21)	903 (23)		
Other	1,095 (17)	747 (19)		
Tumor Size, (mm), n (%)				
≤20	398 (6)	443 (11)	<0.0001	0.9
21–30	680 (11)	537 (14)		
31–50	1,645 (25)	944 (24)		
51–70	1,098 (17)	514 (13)		
>70	820 (13)	399 (10)		
Unknown	1,827 (28)	1,071 (28)		
Stage				
IIIA	3,196 (49)	1,942 (50)	0.78	0.9
IIIB	3,272 (51)	1,966 (50)		
Histology, n (%)				
Adenocarcinoma	1,866 (29)	1,636 (41)	<0.0001	0.9
Squamous cell carcinoma	3,201 (49)	1,472 (38)		
Large cell carcinoma	521 (8)	267 (7)		
Other	880 (14)	533 (14)		
Charlson Comorbidity Score, n (%)				
<1	3,991 (62)	2,214 (57)	<0.0001	0.9

Characteristic	Radiation Therapy (N=6,468)	No Treatment (N=3,908)	*P*-value	
			Unadjusted	Adjusted*
1–2	1,344 (21)	785 (20)		
>2	1,133 (18)	909 (23)		

*Adjusted for propensity score

Table 2

Adjusted Analysis for Risk of Death for Elderly Patients with Unresected Stage III NSCLC Treated with and without Lone Radiotherapy

Analyses	Overall Survival		Lung Cancer-specific Survival	
	Hazard Ratio*	95% CI	Hazard Ratio*	95% CI
All Stage III				
Adjusted model	0.87	0.83–0.91	0.90	0.85–0.93
Stratified by propensity score quintiles	0.86	0.83–0.90	0.88	0.84–0.93
Matched propensity score model	0.89	0.85–0.93	0.90	0.86–0.95
Radiation complexity planning				
Intermediate	1.05	0.99–1.11	1.02	0.97–1.09
Complex	0.83	0.76–0.90	0.87	0.79–0.95
Stage IIIA				
Adjusted model	0.83	0.78–0.88	0.86	0.80–0.92
Stratified by propensity score quintiles	0.83	0.78–0.88	0.85	0.80–0.91
Matched propensity score model	0.83	0.77–0.88	0.87	0.81–0.94
Radiation complexity planning				
Intermediate	1.02	0.94–1.10	1.02	0.93–1.11
Complex	0.82	0.73–0.93	0.86	0.76–0.98
Stage IIIB				
Adjusted model	0.90	0.85–0.96	0.92	0.86–0.98
Stratified by propensity score quintiles	0.89	0.84–0.95	0.91	0.85–0.97
Matched propensity score model	0.96	0.90–1.03	0.95	0.89–1.03
Radiation complexity planning				
Intermediate	1.07	0.99–1.16	1.03	0.95–1.12
Complex	0.83	0.73–0.93	0.87	0.76–0.99

* Hazard of death for patients treated with lone RT versus no RT

CI: Confidence interval

Table 3

Hospital Admissions for Serious Adverse Events among Unresected Elderly Stage III NSCLC patients

Adverse events	Patients admitted with adverse events N (%)		Odds ratio (95% CI)	Adjusted Odds ratio (95% CI)*
	RT	No RT		
Pneumonitis	139 (2.2)	≤11 (≤1) †	85.8 (11.9–613.6)	88.8 (12.4–636.1)
Esophagitis	68 (1.1)	≤11 (≤1) †	8.3 (3.3–20.6)	8.3 (3.3–20.6)

*Adjusted for propensity score

†Exact numbers not reported for patient confidentiality

RT: Radiotherapy CI: Confidence interval